

DOCKET NO.: JJPR-0029 (ORT-1573)
Application No.: 10/056,828
Office Action Dated: August 26, 2003

PATENT
REPLY FILED UNDER EXPEDITED
PROCEDURE PURSUANT TO
37 CFR § 1.116

REMARKS/ARGUMENTS

Claims 1-22 are pending and under examination. With this response, Applicants are resubmitting an Associate Power of Attorney and Change of Correspondence Address and an Associate Power of Attorney that were filed with the United States Patent and Trademark Office on May 19, 2003. Please note this change of address for the next communication.

Formal matters

As of this date, Applicants have not received an initialed copy of page 3 of 5 of the IDS mailed February 25, 2002. Applicants therefore respectfully request an initialed Form 1449.

Rejection under 35 U.S.C. § 103(a)

Claims 1-22 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Shank *et al.* (WO 00/61138 A1) in view of Sachdeo (Topiramate: Clinical Profile in Epilepsy, Clin Pharmacokinet, May 1998, 34(5):335-346) and further in view of Brines *et al.* (WO 00-66164). Applicants respectfully traverse. Applicants assert that the combined teachings of Shank *et al.* (WO 00/61138 A1), Sachdeo (Topiramate: Clinical Profile in Epilepsy, Clin Pharmacokinet, May 1998, 34(5):335-346), and Brines *et al.* (WO 00-66164) do not render the invention of the present application obvious.

With this reply, Applicants attach an expert declaration under 37 C.F.R. § 1.132 by Dr. Carlos R. Plata-Salaman (Exhibit A). This declaration is submitted herewith in order to demonstrate that one of skill in the art, after reading the cited references, would not be motivated to administer both a fructopyranose sulfamate and erythropoietin concomitantly to treat neurological dysfunction in a subject.

Applicants have discovered that when erythropoietin and topiramate are administered concomitantly, the combination of the two agents is such that the total combined effect is greater than the sum of their individual effects, *i.e.*, a synergistic effect is observed. Accordingly, the claims are directed, in part, to methods for treating a neurological dysfunction comprising co-therapy with a therapeutically effective amount of a

fructopyranose sulfamate and erythropoietin. The amount of the fructopyranose sulfamate and the amount of the erythropoietin are selected to produce a *synergistic effect*.

It is well settled in the courts that greater than expected results are evidence of nonobviousness, *See* MPEP 716.02(a). Moreover, evidence of a greater than expected result may be shown by demonstrating synergism, "evidence of a greater than expected result may also be shown by demonstrating an effect which is greater than the sum of each of the effects taken separately (i.e., demonstrating "synergism"). *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir). A showing that the results were greater than those which would have been expected from the prior art to an unobvious extent, and that the results are of significant practical advantage is sufficient to overcome a *prima facie* case of obviousness. *Ex parte The NutraSweet Co.*, 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991).

In the reply dated May 19, 2003, Applicants argued that co-therapy with erythropoietin and topiramate produces unexpected results in that the combination produces a synergistic effect and requested that the rejection under § 103(a) be withdrawn. The present Action maintains the rejection and states that, "one of ordinary skill in the art, when combining active agents known in the art to independently treat identical conditions with correlative concentrations of the active agents, would expect that the results obtained would provide some synergy of action if correlative amounts of each component separately would indeed provide therapy for neurological conditions when combined to provide a co-administration to a patient in need thereof." (Office Action dated August 26, 2003, page 6-7).

The Applicants respectfully disagree with the Action's conclusions and assert that there are compelling reasons why one of skill in the art would not be persuaded to administer the two drugs concomitantly in a treatment protocol. As explained by Dr. Plata-Salaman in his declaration, the underlying reason why one of skill in the art *would not* expect that combination therapy with topiramate and erythropoietin would be desirable for the treatment of neurological conditions is that topiramate and erythropoietin are very different classes of molecules and have distinct features as they relate to chemistry, mechanism of action, pharmacokinetics, and current clinical uses. In his declaration, Dr. Plata-Salaman provides a table exemplifying the very different properties of the two drugs (see Exhibit A).

According to Dr. Plata-Salaman, treatment of neurological or neurodegenerative disorders can involve combination therapy using two or more drugs. Dr. Plata-Salaman further explains, however, that such concomitant therapy requires a specific rationale. When developing a rationale for concomitant therapy, one of skill in the art would look to the characteristics of each individual component, for instance, mechanism of action and pharmacokinetic and metabolic features of the respective compounds. According to Dr. Plata-Salaman, because the mechanism of action and pharmacokinetic and metabolic features of topiramate and erythropoietin are so disparate, one of skill in the art would not be persuaded to administer these two drugs concomitantly. According to Dr. Plata-Salaman, there is no *a priori* support for the notion that two drugs with such different properties would work together to provide even an equivalent effect, let alone a *synergistic* effect in the treatment of neurological disorders.

Moreover, in response to the notion that the cited references can be combined to teach the methods of the present invention, Dr. Plata-Salaman explains that nowhere in the cited art is it suggested that topiramate and erythropoietin have properties that would indicate that they would work together to provide a synergistic effect.

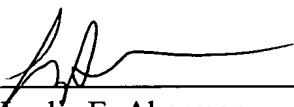
Accordingly, because co-therapy with both erythropoietin and topiramate results in a synergistic effect and because Applicants have demonstrated that it would not be obvious to one of skill in the art of treating neurological or neurodegenerative disorders to administer two drugs having properties as divergent as topiramate and erythropoietin concomitantly to a subject, Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

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Applicants respectfully submit that the foregoing constitutes a *bona fide* attempt to advance prosecution. If a telephonic interview would facilitate advancing prosecution, the undersigned invites the Examiner to call her at the number below.

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